10/524152

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=> d his

     (FILE 'HOME' ENTERED AT 09:08:03 ON 08 AUG 2007)

     FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
     LIFESCI' ENTERED AT 09:15:26 ON 08 AUG 2007
L1            10 S ECTEINASCIDIN (W)COMPOUND?
L2             3 S (BACTER? OR CANDIDA?) AND L1
L3             8 DUP REM L1 (2 DUPLICATES REMOVED)
L4             2 S L3 AND RECOMBINANT
                 E ESTEBAN B P/AU
                 E PEREZ T A/AU
L5           629 S E2-E3
                 E IGLESIAS A V/AU
                 E IGLESIAS ANNA/AU
L6             2 S E3
                 E MORENO R M/AU
L7            49 S E3
L8           680 S L5 OR L6 OR L7
L9             0 S L3 AND L8
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 NEWS  2  MAY 01   New CAS web site launched
 NEWS  3  MAY 08   CA/CAplus Indian patent publication number format defined
 NEWS  4  MAY 14   RDISCLOSURE on STN Easy enhanced with new search and display
                   fields
 NEWS  5  MAY 21   BIOSIS reloaded and enhanced with archival data
 NEWS  6  MAY 21   TOXCENTER enhanced with BIOSIS reload
 NEWS  7  MAY 21   CA/CAplus enhanced with additional kind codes for German
                   patents
 NEWS  8  MAY 22   CA/CAplus enhanced with IPC reclassification in Japanese
                   patents
 NEWS  9  JUN 27   CA/CAplus enhanced with pre-1967 CAS Registry Numbers
 NEWS 10  JUN 29   STN Viewer now available
 NEWS 11  JUN 29   STN Express, Version 8.2, now available
 NEWS 12  JUL 02   LEMBASE coverage updated
 NEWS 13  JUL 02   LMEDLINE coverage updated
 NEWS 14  JUL 02   SCISEARCH enhanced with complete author names
 NEWS 15  JUL 02   CHEMCATS accession numbers revised
 NEWS 16  JUL 02   CA/CAplus enhanced with utility model patents from China
 NEWS 17  JUL 16   CAplus enhanced with French and German abstracts
 NEWS 18  JUL 18   CA/CAplus patent coverage enhanced
 NEWS 19  JUL 26   USPATFULL/USPAT2 enhanced with IPC reclassification
 NEWS 20  JUL 30   USGENE now available on STN
 NEWS 21  AUG 06   CAS REGISTRY enhanced with new experimental property tags
 NEWS 22  AUG 06   BEILSTEIN updated with new compounds
 NEWS 23  AUG 06   FSTA enhanced with new thesaurus edition

 NEWS EXPRESS  29 JUNE 2007:  CURRENT WINDOWS VERSION IS V8.2,
               CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 05 JULY 2007.

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=> file medline embase biosis biotechds scisearch hcaplus ntis lifesci
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         2.52       2.52

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FILE 'BIOTECHDS' ENTERED AT 09:15:26 ON 08 AUG 2007
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FILE 'LIFESCI' ENTERED AT 09:15:26 ON 08 AUG 2007
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=> s ecteinascidin (w)compound?
L1          10 ECTEINASCIDIN (W) COMPOUND?

=> s (bacter? or candida?) and l1
L2           3 (BACTER? OR CANDIDA?) AND L1

=> d 1-3 ibib ab

L2    ANSWER 1 OF 3  BIOTECHDS COPYRIGHT 2007 THE THOMSON CORP. on STN
ACCESSION NUMBER: 2004-18619  BIOTECHDS
TITLE:            Nucleic acid comprising a gene cluster encoding one or more
                  non-ribosomal peptide synthetases which catalyze one or more
                  step of the biosynthesis of safracins is useful for producing
                  a safracin compound or its analogue;
                     recombinant enzyme protein production via plasmid
                     expression in bacterium cell for use in
                     antibiotic production and disease therapy
AUTHOR:           VELASCO IGLESIAS A; DE LA CALLE F; APARICIO PEREZ T;
                  SCHLEISSNER SANCHEZ C; ACEBO PAIS P; RODRIGUEZ RAMOS P; REYES
                  BENITEZ F; HENRIQUEZ PELAEZ R
PATENT ASSIGNEE:  PHARMA MAR SA; RUFFLES G K
PATENT INFO:      WO 2004056998 8 Jul 2004
APPLICATION INFO: WO 2003-GB5563 19 Dec 2003
PRIORITY INFO:    GB 2002-29793 20 Dec 2002; GB 2002-29793 20 Dec 2002
DOCUMENT TYPE:    Patent
LANGUAGE:         English
OTHER SOURCE:     WPI: 2004-543304 [52]
AB    DERWENT ABSTRACT:
      NOVELTY - A nucleic acid sequence (I) comprising a nucleic acid sequence
      encoding one or more non-ribosomal peptide synthetases which catalyze one
      or more step of the biosynthesis of safracins, a nucleic acid sequence
```

which is complementary to the sequence, or variants or portions of any of the sequences, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) a hybridization probe (II) comprising (I); (2) a polypeptide (III) encoded by (I); (3) a vector (IV) comprising (I); (4) a host cell (V) transformed with one or more of (I), or comprising (IV); (5) producing (M1) a safracin compound or its analogue; (6) a composition (VI) comprising (I); (7) use of P2, P14 analogs and its derivatives (VII) in combinatorial biosynthesis of one or more of non-ribosomal peptide synthetases, diketopiperazine rings and safracins; (8) a safracin compound (VIII) obtained by (M1); and (9) a pharmaceutical composition (IX) comprising (VIII) and a diluent, carrier or excipient.

BIOTECHNOLOGY - Preferred Nucleic Acid: (I) is gene cluster having open reading frames, which encode polypeptides sufficient to direct the synthesis of a safracin molecule. (I) comprises a fully defined sequence (SEQ ID NO:1) of 26705 nucleotides as given in the specification. (I) comprises one or more of sacA, sacB, sacC, sacD, sacE, sacF, sacG, sacH, sacI, sacJ, orf1, orf2, orf3 or orf4 genes, including its variant or portion. (I) encodes a polypeptide which is at least 30% identical in amino acid sequence to a polypeptide encoded by any of the safracin gene cluster open reading frames sacA to sacJ and orf1 to orf4 or encoded by its variant or portions. (I) encodes any one of SacA, SacB, SacC, SacD, SacE, SacF, SacG, SacH, SacI, SacJ, Orf1, Orf2, Orf3 or Orf4 proteins and its variants, mutants or portions. The encodes proteins comprises any one of 14 amino acid sequences e.g., a fully defined sequence (SEQ ID NO:2-15) of 1004, 1062, 1432, 350, 61, 355, 347, 180, 220, 509, 348, 572, 230 or 348 amino acids as given in the specification. (I) encodes a peptide synthetase, a L-Tyr derivative hydroxylase, a L-Tyr derivative methylase, a L-Tyr O-methylase, a methyl-transferase or a monooxygenase or a safracin resistance protein. (I) is 50 nucleotides in length, or is between 100-5000 or 100-2500 nucleotides in length. Preferred Probe: (II) comprises 10 or more nucleotides, or 25-60 nucleotides. Preferred Polypeptide: (III) comprises any one of (SEQ ID NO:2-15). Preferred Vector: (IV) is an expression vector or cosmid. Preferred Host Cell: (V) is transformed with an exogenous nucleic acid comprising a gene cluster encoding polypeptides sufficient to direct the synthesis of a safracin. (V) is a microorganism e.g., bacterium. In a recombinant bacterial host cell, at least a portion of (I) is disrupted to result in a recombinant host cell that produces altered levels of safracin compound or safracin analogue, relative to a corresponding non-recombinant bacterial host cell. The disrupted nucleic acid sequence is endogenous. Preferred Method: In (M1), the method may comprise fermenting an organism (preferably Pseudomonas sp.) in which the copy number of the gene cluster has been increased. Alternatively, the method may comprise fermenting an organism (Pseudomonas sp.) in which the expression of (I) has been modulated by manipulation or replacement of one or more gene or sequence responsible for regulating expression. Furthermore, the method may comprises contacting a compound that is a substrate for a polypeptide encoded by one or more of the open reading frames of (I), where the polypeptide chemically modifies the compound. Preferred Compound: (VIII) has any of the structural formulas as given.

ACTIVITY - Cytostatic; Antimicrobial. No supporting data available.

MECHANISM OF ACTION - None given.

USE - (I) is useful for producing a safracin compound or its analogue. (I) is also useful for the combinatorial biosynthesis of one or more of non-ribosomal peptide synthetases, diketopiperazine rings and safracins. The safracin compound (VIII) is useful as an antitumor agent, as an antimicrobial agent, for producing medicament for the treatment of cancer or microbial infections, or in the synthesis of ecteinascidin compounds. The hybridization probe (II) is useful for detecting safracin or ecteinascidin gene that is conducted in Ecteinascidia turbinate (all claimed).

EXAMPLE - No relevant example is given. (127 pages)

L2 ANSWER 2 OF 3 BIOTECHDS COPYRIGHT 2007 THE THOMSON CORP. on STN
ACCESSION NUMBER: 2004-09640 BIOTECHDS
TITLE: New Candidatus Endoecteinascidia frumentensis, useful in biosynthesizing of ecteinascidin compound and in developing antitumoral agent; recombinant protein production for use in ecteinascidin preparation
AUTHOR: PEREZ ESTEBAN B; APARICIO PEREZ T; VELASCO IGLESIAS A; HENRIQUEZ PELAEZ R; MUNOZ MORENO R; MOSS C; MCKENZIE D
PATENT ASSIGNEE: PHARMA MAR SAU
PATENT INFO: WO 2004015143 19 Feb 2004
APPLICATION INFO: WO 2003-GB3538 13 Aug 2003
PRIORITY INFO: GB 2002-18813 13 Aug 2002; GB 2002-18813 13 Aug 2002
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2004-180692 [17]
AB DERWENT ABSTRACT:
NOVELTY - An isolated polynucleotide (I), is new.

DETAILED DESCRIPTION - An isolated polynucleotide (I), is new. (I) comprises: (a) a sequence of 1502 bp (SEQ ID NO: 1) or its a modification, variant or fragment; (b) a sequence having at least 50% identity to (a); (c) a sequence capable of hybridizing to (a) or (b) under stringent conditions; or (d) a fragment of a polynucleotide sequence of (a)-(c). INDEPENDENT CLAIMS are also included for: (1) a polynucleotide fragment comprises at least 5, 10, 15, 20, 25, 30 or more contiguous nucleotides of (I); (2) a probe or primer comprising or consisting of a polynucleotide fragment of (1); (3) a recombinant DNA comprising or consisting of (I); and (4) an isolated bacterium including (I).

WIDER DISCLOSURE - Also disclosed is a process for amplifying DNA molecule.

BIOTECHNOLOGY - Preferred Polynucleotide: (I) comprises a sequence having at least 70%, 75%, 85%, 90%, 95% or 97% identity with SEQ ID NO: 1 or its hybridized sequence or fragment. Preferred Bacterium: The bacterium is Candidatus Endoecteinascidia frumentensis.

ACTIVITY - Cytostatic. No biological data given.

MECHANISM OF ACTION - None given.

USE - The polynucleotide and polypeptides are useful in biosynthesizing of ecteinascidin compound and in developing antitumoral agent.

EXAMPLE - Two different universal 16S rDNA bacterial PCR set of primers and one set of specific oligonucleotides for DNA sequences of Candidatus Endoecteinascidia frumentensis were used for amplification and run for PCR. The PCR product was confirmed by agarose gel electrophoresis and ethidium bromide staining. PCR products were then purified, transformed into competent E. coli DH5alpha and cloned. Putative insert-containing clones were elected. PCR reaction was performed and confirmed by agarose gel electrophoresis. Positive PCR products were precipitated and resuspended. restriction fragment full-length polymorphism analysis was carried out. Plasmid DAN was isolated and sequenced giving a 1052 bp sequence. (38 pages)

L2 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:143318 HCAPLUS
DOCUMENT NUMBER: 140:196190
TITLE: Endoecteinascidia frumentensis, an endosymbiont of Ecteinascidia turbinata
INVENTOR(S): Perez Esteban, Beatriz; Aparicio Perez, Tomas; Velasco Iglesias, Ana; Henriquez Pelaez, Ruben; Munoz Moreno, Rosario; Moss, Claire; McKenzie, Douglas
PATENT ASSIGNEE(S): Pharma Mar, S.A.U., Spain
SOURCE: PCT Int. Appl., 38 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004015143	A2	20040219	WO 2003-GB3538	20030813
WO 2004015143	A3	20040415		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2003251060	A1	20040225	AU 2003-251060	20030813
EP 1532280	A2	20050525	EP 2003-784299	20030813

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

US 2006167228	A1	20060727	US 2005-524152	20050824
PRIORITY APPLN. INFO.:			GB 2002-18813 A	20020813
			WO 2003-GB3538 W	20030813

AB RDNA corresponding to an endosymbiotic bacteria associated with Ecteinascidia turbinata has been identified. The bacterium appears to be responsible for the biosynthesis of ecteinascidin compds. The 16S rDNA sequence corresponding to Candidatus Endoecteinascidia frumentensis SEQ ID NO: 1 has been deposited in GeneBank with the accession number AY054370.

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FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS, LIFESCI' ENTERED AT 09:15:26 ON 08 AUG 2007
L1 10 S ECTEINASCIDIN (W)COMPOUND?
L2 3 S (BACTER? OR CANDIDA?) AND L1

=> dup rem l1
PROCESSING COMPLETED FOR L1
L3 8 DUP REM L1 (2 DUPLICATES REMOVED)

=> d 1-8 ibib ab

L3 ANSWER 1 OF 8 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:319213 HCAPLUS
DOCUMENT NUMBER: 144:343581
TITLE: Ecteinascidin compounds as anti-inflammatory agents
INVENTOR(S): Allavena, Paola; D'Incalci, Maurizio; Faircloth, Glynn Thomas
PATENT ASSIGNEE(S): Pharma Mar S.A., Sociedad Unipersonal, Spain; Ruffles, Graham Keith
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006035244	A2	20060406	WO 2005-GB50164	20050928
WO 2006035244	A3	20060831		
WO 2006035244	A9	20070301		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

AU 2005288696	A1	20060406	AU 2005-288696	20050928
CA 2583464	A1	20060406	CA 2005-2583464	20050928
EP 1812114	A2	20070801	EP 2005-805089	20050928

R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU

PRIORITY APPLN. INFO.: US 2004-614093P P 20040928
WO 2005-GB50164 W 20050928

OTHER SOURCE(S): MARPAT 144:343581

AB The anti-inflammatory activity of ecteinascidin compds . was determined Ecteinascidin 743 (I) and other ecteinascidin compds. affect viability and functions of monocyte/macophages. Examples include noncytotoxic concs. of I inhibit in vitro and in vivo macrophage differentiation, I shows selective cytotoxic effect on mononuclear phagocytes, I inhibits the production of inflammatory cytokines/chemokines, and I was compared with antineoplastic agents currently used in ovarian cancer.

L3 ANSWER 2 OF 8 BIOTECHDS COPYRIGHT 2007 THE THOMSON CORP. on STN
DUPLICATE 1

ACCESSION NUMBER: 2004-09640 BIOTECHDS

TITLE: New Candidatus Endoecteinascidia frumentensis, useful in biosynthesizing of ecteinascidin compound and in developing antitumoral agent; recombinant protein production for use in ecteinascidin preparation

AUTHOR: PEREZ ESTEBAN B; APARICIO PEREZ T; VELASCO IGLESIAS A; HENRIQUEZ PELAEZ R; MUNOZ MORENO R; MOSS C; MCKENZIE D

PATENT ASSIGNEE: PHARMA MAR SAU

PATENT INFO: WO 2004015143 19 Feb 2004

APPLICATION INFO: WO 2003-GB3538 13 Aug 2003

PRIORITY INFO: GB 2002-18813 13 Aug 2002; GB 2002-18813 13 Aug 2002

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 2004-180692 [17]

AB DERWENT ABSTRACT:

NOVELTY - An isolated polynucleotide (I), is new.

DETAILED DESCRIPTION - An isolated polynucleotide (I), is new. (I) comprises: (a) a sequence of 1502 bp (SEQ ID NO: 1) or its a modification, variant or fragment; (b) a sequence having at least 50% identity to (a); (c) a sequence capable of hybridizing to (a) or (b) under stringent conditions; or (d) a fragment of a polynucleotide sequence of (a)-(c). INDEPENDENT CLAIMS are also included for: (1) a polynucleotide fragment comprises at least 5, 10, 15, 20, 25, 30 or more contiguous nucleotides of (I); (2) a probe or primer comprising or consisting of a polynucleotide fragment of (1); (3) a recombinant DNA

comprising or consisting of (I); and (4) an isolated bacterium including (I).

WIDER DISCLOSURE - Also disclosed is a process for amplifying DNA molecule.

BIOTECHNOLOGY - Preferred Polynucleotide: (I) comprises a sequence having at least 70%, 75%, 85%, 90%, 95% or 97% identity with SEQ ID NO: 1 or its hybridized sequence or fragment. Preferred Bacterium: The bacterium is Candidatus Endoecteinascidia frumentensis.

ACTIVITY - Cytostatic. No biological data given.

MECHANISM OF ACTION - None given.

USE - The polynucleotide and polypeptides are useful in biosynthesizing of ecteinascidin compound and in developing antitumoral agent.

EXAMPLE - Two different universal 16S rDNA bacterial PCR set of primers and one set of specific oligonucleotides for DNA sequences of Candidatus Endoecteinascidia frumentensis were used for amplification and run for PCR. The PCR product was confirmed by agarose gel electrophoresis and ethidium bromide staining. PCR products were then purified, transformed into competent E. coli DH5alpha and cloned. Putative insert-containing clones were elected. PCR reaction was performed and confirmed by agarose gel electrophoresis. Positive PCR products were precipitated and resuspended. restriction fragment full-length polymorphism analysis was carried out. Plasmid DAN was isolated and sequenced giving a 1052 bp sequence. (38 pages)

L3 ANSWER 3 OF 8 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2004:468945 BIOSIS
DOCUMENT NUMBER: PREV200400474017
TITLE: Synthetic process for an intermediate for ecteinascidin and phthalascidin compounds.
AUTHOR(S): Corey, Elias J. [Inventor, Reprint Author]
CORPORATE SOURCE: ASSIGNEE: President and Fellows of Harvard College
PATENT INFORMATION: US 6815544 20041109
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Nov 9 2004) Vol. 1288, No. 2. http://www.uspto.gov/web/menu/patdata.html. e-file. ISSN: 0098-1133 (ISSN print).
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 9 Dec 2004
Last Updated on STN: 9 Dec 2004
AB An efficient process is described for the synthesis of 5, a key intermediate for the synthesis of the potent antitumor agents ecteinascidin 743 (1) and phthalascidin (2) from the readily available building blocks 3b and 4. ##STR1##

L3 ANSWER 4 OF 8 BIOTECHDS COPYRIGHT 2007 THE THOMSON CORP. on STN
ACCESSION NUMBER: 2004-18619 BIOTECHDS
TITLE: Nucleic acid comprising a gene cluster encoding one or more non-ribosomal peptide synthetases which catalyze one or more step of the biosynthesis of safracins is useful for producing a safracin compound or its analogue;
recombinant enzyme protein production via plasmid expression in bacterium cell for use in antibiotic production and disease therapy
AUTHOR: VELASCO IGLESIAS A; DE LA CALLE F; APARICIO PEREZ T; SCHLEISSNER SANCHEZ C; ACEBO PAIS P; RODRIGUEZ RAMOS P; REYES BENITEZ F; HENRIQUEZ PELAEZ R
PATENT ASSIGNEE: PHARMA MAR SA; RUFFLES G K
PATENT INFO: WO 2004056998 8 Jul 2004
APPLICATION INFO: WO 2003-GB5563 19 Dec 2003
PRIORITY INFO: GB 2002-29793 20 Dec 2002; GB 2002-29793 20 Dec 2002
DOCUMENT TYPE: Patent
LANGUAGE: English

OTHER SOURCE: WPI: 2004-543304 [52]

AB DERWENT ABSTRACT:

NOVELTY - A nucleic acid sequence (I) comprising a nucleic acid sequence encoding one or more non-ribosomal peptide synthetases which catalyze one or more step of the biosynthesis of safracins, a nucleic acid sequence which is complementary to the sequence, or variants or portions of any of the sequences, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) a hybridization probe (II) comprising (I); (2) a polypeptide (III) encoded by (I); (3) a vector (IV) comprising (I); (4) a host cell (V) transformed with one or more of (I), or comprising (IV); (5) producing (M1) a safracin compound or its analogue; (6) a composition (VI) comprising (I); (7) use of P2, P14 analogs and its derivatives (VII) in combinatorial biosynthesis of one or more of non-ribosomal peptide synthetases, diketopiperazine rings and safracins; (8) a safracin compound (VIII) obtained by (M1); and (9) a pharmaceutical composition (IX) comprising (VIII) and a diluent, carrier or excipient.

BIOTECHNOLOGY - Preferred Nucleic Acid: (I) is gene cluster having open reading frames, which encode polypeptides sufficient to direct the synthesis of a safracin molecule. (I) comprises a fully defined sequence (SEQ ID NO:1) of 26705 nucleotides as given in the specification. (I) comprises one or more of sacA, sacB, sacC, sacD, sacE, sacF, sacG, sacH, sacI, sacJ, orf1, orf2, orf3 or orf4 genes, including its variant or portion. (I) encodes a polypeptide which is at least 30% identical in amino acid sequence to a polypeptide encoded by any of the safracin gene cluster open reading frames sacA to sacJ and orf1 to orf4 or encoded by its variant or portions. (I) encodes any one of SacA, SacB, SacC, SacD, SacE, SacF, SacG, SacH, SacI, SacJ, Orf1, Orf2, Orf3 or Orf4 proteins and its variants, mutants or portions. The encodes proteins comprises any one of 14 amino acid sequences e.g., a fully defined sequence (SEQ ID NO:2-15) of 1004, 1062, 1432, 350, 61, 355, 347, 180, 220, 509, 348, 572, 230 or 348 amino acids as given in the specification. (I) encodes a peptide synthetase, a L-Tyr derivative hydroxylase, a L-Tyr derivative methylase, a L-Tyr O-methylase, a methyl-transferase or a monooxygenase or a safracin resistance protein. (I) is 50 nucleotides in length, or is between 100-5000 or 100-2500 nucleotides in length. Preferred Probe: (II) comprises 10 or more nucleotides, or 25-60 nucleotides. Preferred Polypeptide: (III) comprises any one of (SEQ ID NO:2-15). Preferred Vector: (IV) is an expression vector or cosmid. Preferred Host Cell: (V) is transformed with an exogenous nucleic acid comprising a gene cluster encoding polypeptides sufficient to direct the synthesis of a safracin. (V) is a microorganism e.g., bacterium. In a recombinant bacterial host cell, at least a portion of (I) is disrupted to result in a recombinant host cell that produces altered levels of safracin compound or safracin analogue, relative to a corresponding non-recombinant bacterial host cell. The disrupted nucleic acid sequence is endogenous. Preferred Method: In (M1), the method may comprise fermenting an organism (preferably Pseudomonas sp.) in which the copy number of the gene cluster has been increased. Alternatively, the method may comprise fermenting an organism (Pseudomonas sp.) in which the expression of (I) has been modulated by manipulation or replacement of one or more gene or sequence responsible for regulating expression. Furthermore, the method may comprises contacting a compound that is a substrate for a polypeptide encoded by one or more of the open reading frames of (I), where the polypeptide chemically modifies the compound. Preferred Compound: (VIII) has any of the structural formulas as given.

ACTIVITY - Cytostatic; Antimicrobial. No supporting data available.

MECHANISM OF ACTION - None given.

USE - (I) is useful for producing a safracin compound or its analogue. (I) is also useful for the combinatorial biosynthesis of one or more of non-ribosomal peptide synthetases, diketopiperazine rings and safracins. The safracin compound (VIII) is useful as an antitumor agent, as an antimicrobial agent, for producing medicament for the treatment of cancer or microbial infections, or in the synthesis of

ecteinascidin compounds. The hybridization probe (II) is useful for detecting safracin or ecteinascidin gene that is conducted in Ecteinascidia turbinate (all claimed).
EXAMPLE - No relevant example is given. (127 pages)

L3 ANSWER 5 OF 8 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 2

ACCESSION NUMBER: 2004:1014997 SCISEARCH
THE GENUINE ARTICLE: 870PR
TITLE: In vitro culture of the ascidian Ecteinascidia turbinata to supply the antitumor compounds ecteinascidins
AUTHOR: Duckworth A R (Reprint); Samples G A; Wright A E; Pomponi S A
CORPORATE SOURCE: Australian Inst Marine Sci, PMB 3, Townsville, Qld 4810, Australia (Reprint); Harbor Branch Oceanog Inst Inc, Div Biomed Marine Res, Ft Pierce, FL 34946 USA
a.duckworth@aims.gov.au
COUNTRY OF AUTHOR: Australia; USA
SOURCE: AQUACULTURE, (26 NOV 2004) Vol. 241, No. 1-4, pp. 427-439. ISSN: 0044-8486.
PUBLISHER: ELSEVIER SCIENCE BV, PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 18
ENTRY DATE: Entered STN: 16 Dec 2004
Last Updated on STN: 16 Dec 2004
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB In vitro culture of the ascidian Ecteinascidia turbinata is one possible method for supplying ecteinascidins, compounds that have strong antitumor properties. However, appropriate feeding regimes that maximize both zooid growth and biosynthesis of ecteinascidins need to be determined. In one experiment lasting 51 days, E. turbinata colonies were fed mono- and multispecific diets of three microalgae species, Chaetoceros gracilis, Isochrysis galbana, and Nannochloropsis sp., at an initial concentration of 80,000 cells ml(-1). Growth (zooid number per colony and mean zooid length) was greatest overall for colonies fed a monospecific diet of L galbana or a mixed diet of C gracilis and I. galbana, probably because these two diets best met the nutritional requirements of E. turbinata. In a separate experiment lasting 31 days, E. turbinata colonies were fed the two best diets at three cell concentrations: 80,000; 160,000; and 320,000 cells ml-1. Final zooid number per colony was greatest for E. turbinata fed the two highest food concentrations, while final zooid length was greatest on the mixed diet of C gracilis and L galbana. The production of ecteinascidins per colony (mug) was also significantly affected by the feeding regime, being greatest for ascidians fed microalgae at 160,000 and 320,000 cells ml(-1). Ectemascidin production for ascidians fed at the two highest cell concentrations showed a tenfold increase over 31 days, thus indicating that in vitro culture is one possible method of supplying the antitumor compound. Overall, this study suggests that a mixed diet of C gracilis and L galbana at a concentration of 160,000 cells ml(-1) is a good feeding regime for the in vitro culture of E. turbinata to supply ecteinascidins.

L3 ANSWER 6 OF 8 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2000:292350 BIOSIS
DOCUMENT NUMBER: PREV200000292350
TITLE: Nucleophile substituted ecteinascidins and N-oxide ecteinascidins.
AUTHOR(S): Rinehart, Kenneth L. [Inventor, Reprint author]; Zhou, Tong [Inventor]
CORPORATE SOURCE: 1306 S. Carle Ave., Urbana, IL, USA
PATENT INFORMATION: US 5985876 19991116

SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Nov. 16, 1999) Vol. 1228, No. 3. e-file. CODEN: OGUPE7. ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 6 Jul 2000
Last Updated on STN: 7 Jan 2002

AB Five new nucleophile substituted ecteinascidin (Et) compounds have been isolated from extracts of Ecteinascidia turbinata. These compounds have been purified by chromatographic techniques and their structures and bioactivities have been determined. The five nucleophile substituted Et compounds have been designated herein as Et 802 (1), Et 788 (2), Et 760 (3), Et 858 (4) and Et 815 (5). Also obtained were three new N-oxide ecteinascidin compounds, which have been designated herein as Et 717 (6), Et 775 (7) and Et 789 (8). Some of these newly discovered Et compounds show exceedingly potent cytotoxicity against L1210.

L3 ANSWER 7 OF 8 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:706050 HCAPLUS
DOCUMENT NUMBER: 129:326085
TITLE: Nucleophile substituted ecteinascidins and N-oxide ecteinascidins from Ecteinascidia turbinata for tumor treatment, and pharmaceutical and veterinary compositions
INVENTOR(S): Rinehart, Kenneth L.; Zhou, Tong
PATENT ASSIGNEE(S): The Board of Trustees of the University of Illinois, USA
SOURCE: PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9846080	A1	19981022	WO 1998-US7340	19980414
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5985876	A	19991116	US 1998-58499	19980410
CA 2286796	A1	19981022	CA 1998-2286796	19980414
AU 9871114	A	19981111	AU 1998-71114	19980414
AU 747303	B2	20020616		
EP 975218	A1	20000202	EP 1998-918132	19980414
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
BR 9808588	A	20000523	BR 1998-8588	19980414
JP 2001523228	T	20011120	JP 1998-544140	19980414
HU 200103590	A2	20020128	HU 2001-3590	19980414
HU 200103590	A3	20020729		
EP 1668985	A2	20060614	EP 2006-4129	19980414
EP 1668985	A3	20061122		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
NO 9905016	A	19991210	NO 1999-5016	19991014
MX 9909503	A	20000831	MX 1999-9503	19991015
PRIORITY APPLN. INFO.:			US 1997-43596P P	19970415

EP 1998-918132 A3 19980414
WO 1998-US7340 W 19980414

AB Five new nucleophile substituted ecteinascidin (Et) compds. have been isolated from exts. of Ecteinascidia turbinata. These compds. have been purified by chromatog. techniques and their structures and bioactivities have been determined The five nucleophile substituted Et compds. have been designated herein as Et 802, Et 788, Et 760, Et 858, and Et 815. Also obtained were three new N-oxide ecteinascidin compds., which have been designated herein as Et 717, Et 775, and Et 789. Some of these newly discovered Et compds. show exceedingly potent cytotoxicity against L1210.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 8 OF 8 BIOTECHDS COPYRIGHT 2007 THE THOMSON CORP. on STN
ACCESSION NUMBER: 1988-03399 BIOTECHDS
TITLE: New ecteinascidin compounds extracted from Ecteinascidia turbinata; with antibiotic and cytostatic activities
PATENT ASSIGNEE: Univ.Illinois
PATENT INFO: WO 8707610 17 Dec 1987
APPLICATION INFO: WO 1987-US1226 1 Jun 1987
PRIORITY INFO: US 1987-6395 23 Jan 1987; US 1986-872189 9 Jun 1986
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 1987-362705 [51]

AB The compounds ecteinascidins 729, 743, 745, 759A, 759B and 770 are new. They have been analyzed by UV, PMR and fast atom bombardment MS etc., and are obtained from the marine tunicate Ecteinascidia turbinata. The compounds have antibiotic and, in some cases, cytostatic/antileukemia activities. They may be formulated for human or veterinary medicine. Frozen tunicates were thawed and the solid fraction extracted with MeOH in a blender. The extract was treated with aqueous NaNO3 and toluene to form a 2-phase system. The aqueous phase was extracted 3 times with toluene and the toluene fractions were evaporated. The residual aqueous phase was extracted 9 times with dichloromethane and the extracts evaporated to an oil. This was solubilized with dichloromethane and methanol, and the solution evaporated to give a residue which was triturated with hexane and dichloromethane. The latter triturate was purified by countercurrent chromatography to give 8 fractions. 2 Bioactive fractions were chromatographed on CHP-20 porous polymer and then on Partisil 10 ODS-3 to give the ecteinascidins. (31pp)

=> d his

(FILE 'HOME' ENTERED AT 09:08:03 ON 08 AUG 2007)

FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS, LIFESCI' ENTERED AT 09:15:26 ON 08 AUG 2007
L1 10 S ECTEINASCIDIN (W)COMPOUND?
L2 3 S (BACTER? OR CANDIDA?) AND L1
L3 8 DUP REM L1 (2 DUPLICATES REMOVED)

=> s l3 and recombinant
L4 2 L3 AND RECOMBINANT

=> d 1-2 ibib ab

L4 ANSWER 1 OF 2 BIOTECHDS COPYRIGHT 2007 THE THOMSON CORP. on STN
ACCESSION NUMBER: 2004-18619 BIOTECHDS
TITLE: Nucleic acid comprising a gene cluster encoding one or more non-ribosomal peptide synthetases which catalyze one or more step of the biosynthesis of safracins is useful for producing

a safracin compound or its analogue; recombinant enzyme protein production via plasmid expression in bacterium cell for use in antibiotic production and disease therapy

AUTHOR: VELASCO IGLESIAS A; DE LA CALLE F; APARICIO PEREZ T; SCHLEISSNER SANCHEZ C; ACEBO PAIS P; RODRIGUEZ RAMOS P; REYES BENITEZ F; HENRIQUEZ PELAEZ R

PATENT ASSIGNEE: PHARMA MAR SA; RUFFLES G K

PATENT INFO: WO 2004056998 8 Jul 2004

APPLICATION INFO: WO 2003-GB5563 19 Dec 2003

PRIORITY INFO: GB 2002-29793 20 Dec 2002; GB 2002-29793 20 Dec 2002

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 2004-543304 [52]

AB DERWENT ABSTRACT:

NOVELTY - A nucleic acid sequence (I) comprising a nucleic acid sequence encoding one or more non-ribosomal peptide synthetases which catalyze one or more step of the biosynthesis of safracins, a nucleic acid sequence which is complementary to the sequence, or variants or portions of any of the sequences, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) a hybridization probe (II) comprising (I); (2) a polypeptide (III) encoded by (I); (3) a vector (IV) comprising (I); (4) a host cell (V) transformed with one or more of (I), or comprising (IV); (5) producing (M1) a safracin compound or its analogue; (6) a composition (VI) comprising (I); (7) use of P2, P14 analogs and its derivatives (VII) in combinatorial biosynthesis of one or more of non-ribosomal peptide synthetases, diketopiperazine rings and safracins; (8) a safracin compound (VIII) obtained by (M1); and (9) a pharmaceutical composition (IX) comprising (VIII) and a diluent, carrier or excipient.

BIOTECHNOLOGY - Preferred Nucleic Acid: (I) is gene cluster having open reading frames, which encode polypeptides sufficient to direct the synthesis of a safracin molecule. (I) comprises a fully defined sequence (SEQ ID NO:1) of 26705 nucleotides as given in the specification. (I) comprises one or more of sacA, sacB, sacC, sacD, sacE, sacF, sacG, sacH, sacI, sacJ, orf1, orf2, orf3 or orf4 genes, including its variant or portion. (I) encodes a polypeptide which is at least 30% identical in amino acid sequence to a polypeptide encoded by any of the safracin gene cluster open reading frames sacA to sacJ and orf1 to orf4 or encoded by its variant or portions. (I) encodes any one of SacA, SacB, SacC, SacD, SacE, SacF, SacG, SacH, SacI, SacJ, Orf1, Orf2, Orf3 or Orf4 proteins and its variants, mutants or portions. The encodes proteins comprises any one of 14 amino acid sequences e.g., a fully defined sequence (SEQ ID NO:2-15) of 1004, 1062, 1432, 350, 61, 355, 347, 180, 220, 509, 348, 572, 230 or 348 amino acids as given in the specification. (I) encodes a peptide synthetase, a L-Tyr derivative hydroxylase, a L-Tyr derivative methylase, a L-Tyr O-methylase, a methyl-transferase or a monooxygenase or a safracin resistance protein. (I) is 50 nucleotides in length, or is between 100-5000 or 100-2500 nucleotides in length. Preferred Probe: (II) comprises 10 or more nucleotides, or 25-60 nucleotides. Preferred Polypeptide: (III) comprises any one of (SEQ ID NO:2-15). Preferred Vector: (IV) is an expression vector or cosmid. Preferred Host Cell: (V) is transformed with an exogenous nucleic acid comprising a gene cluster encoding polypeptides sufficient to direct the synthesis of a safracin. (V) is a microorganism e.g., bacterium. In a recombinant bacterial host cell, at least a portion of (I) is disrupted to result in a recombinant host cell that produces altered levels of safracin compound or safracin analogue, relative to a corresponding non-recombinant bacterial host cell. The disrupted nucleic acid sequence is endogenous. Preferred Method: In (M1), the method may comprise fermenting an organism (preferably Pseudomonas sp.) in which the copy number of the gene cluster has been increased. Alternatively, the method may comprise fermenting an organism (Pseudomonas sp.) in which the expression of (I) has been modulated by manipulation or replacement of

one or more gene or sequence responsible for regulating expression. Furthermore, the method may comprises contacting a compound that is a substrate for a polypeptide encoded by one or more of the open reading frames of (I), where the polypeptide chemically modifies the compound. Preferred Compound: (VIII) has any of the structural formulas as given.

ACTIVITY - Cytostatic; Antimicrobial. No supporting data available.

MECHANISM OF ACTION - None given.

USE - (I) is useful for producing a safracin compound or its analogue. (I) is also useful for the combinatorial biosynthesis of one or more of non-ribosomal peptide synthetases, diketopiperazine rings and safracins. The safracin compound (VIII) is useful as an antitumor agent, as an antimicrobial agent, for producing medicament for the treatment of cancer or microbial infections, or in the synthesis of ecteinascidin compounds. The hybridization probe (II) is useful for detecting safracin or ecteinascidin gene that is conducted in Ecteinascidia turbinate (all claimed).

EXAMPLE - No relevant example is given. (127 pages)

L4 ANSWER 2 OF 2 BIOTECHDS COPYRIGHT 2007 THE THOMSON CORP. on STN
ACCESSION NUMBER: 2004-09640 BIOTECHDS
TITLE: New Candidatus Endoecteinascidia frumentensis, useful in biosynthesizing of ecteinascidin compound and in developing antitumoral agent; recombinant protein production for use in ecteinascidin preparation
AUTHOR: PEREZ ESTEBAN B; APARICIO PEREZ T; VELASCO IGLESIAS A; HENRIQUEZ PELAEZ R; MUNOZ MORENO R; MOSS C; MCKENZIE D
PATENT ASSIGNEE: PHARMA MAR SAU
PATENT INFO: WO 2004015143 19 Feb 2004
APPLICATION INFO: WO 2003-GB3538 13 Aug 2003
PRIORITY INFO: GB 2002-18813 13 Aug 2002; GB 2002-18813 13 Aug 2002
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2004-180692 [17]
AB DERWENT ABSTRACT:

NOVELTY - An isolated polynucleotide (I), is new.

DETAILED DESCRIPTION - An isolated polynucleotide (I), is new. (I) comprises: (a) a sequence of 1502 bp (SEQ ID NO: 1) or its a modification, variant or fragment; (b) a sequence having at least 50% identity to (a); (c) a sequence capable of hybridizing to (a) or (b) under stringent conditions; or (d) a fragment of a polynucleotide sequence of (a)-(c). INDEPENDENT CLAIMS are also included for: (1) a polynucleotide fragment comprises at least 5, 10, 15, 20, 25, 30 or more contiguous nucleotides of (I); (2) a probe or primer comprising or consisting of a polynucleotide fragment of (1); (3) a recombinant DNA comprising or consisting of (I); and (4) an isolated bacterium including (I).

WIDER DISCLOSURE - Also disclosed is a process for amplifying DNA molecule.

BIOTECHNOLOGY - Preferred Polynucleotide: (I) comprises a sequence having at least 70%, 75%, 85%, 90%, 95% or 97% identity with SEQ ID NO: 1 or its hybridized sequence or fragment. Preferred Bacterium: The bacterium is Candidatus Endoecteinascidia frumentensis.

ACTIVITY - Cytostatic. No biological data given.

MECHANISM OF ACTION - None given.

USE - The polynucleotide and polypeptides are useful in biosynthesizing of ecteinascidin compound and in developing antitumoral agent.

EXAMPLE - Two different universal 16S rDNA bacterial PCR set of primers and one set of specific oligonucleotides for DNA sequences of Candidatus Endoecteinascidia frumentensis were used for amplification and run for PCR. The PCR product was confirmed by agarose gel electrophoresis and ethidium bromide staining. PCR products were then purified, transformed into competent E. coli DH5alpha and cloned. Putative

insert-containing clones were elected. PCR reaction was performed and confirmed by agarose gel electrophoresis. Positive PCR products were precipitated and resuspended. restriction fragment full-length polymorphism analysis was carried out. Plasmid DAN was isolated and sequenced giving a 1052 bp sequence. (38 pages)

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=> d his

     (FILE 'HOME' ENTERED AT 09:08:03 ON 08 AUG 2007)

     FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
     LIFESCI' ENTERED AT 09:15:26 ON 08 AUG 2007
L1            10 S ECTEINASCIDIN (W)COMPOUND?
L2             3 S (BACTER? OR CANDIDA?) AND L1
L3             8 DUP REM L1 (2 DUPLICATES REMOVED)
L4             2 S L3 AND RECOMBINANT

=> e esteban b p/au
E1            23      ESTEBAN B M/AU
E2             1      ESTEBAN B N A/AU
E3             0 --> ESTEBAN B P/AU
E4             3      ESTEBAN BARRAGAN M A/AU
E5             3      ESTEBAN BARRAGAN MIGUEL A/AU
E6             1      ESTEBAN BARRANCO F/AU
E7             1      ESTEBAN BARRIOS B/AU
E8             1      ESTEBAN BASILIO MORENO/AU
E9             1      ESTEBAN BEATRIZ MEANA/AU
E10            2      ESTEBAN BEATRIZ N A/AU
E11            1      ESTEBAN BELASCO EDUARDO/AU
E12            1      ESTEBAN BENAVIDES B/AU

=> e perez t a/au
E1            17      PEREZ SYLVIE/AU
E2           625      PEREZ T/AU
E3             4 --> PEREZ T A/AU
E4             2      PEREZ T A T/AU
E5             2      PEREZ T ALDEIMA T/AU
E6             4      PEREZ T B/AU
E7             1      PEREZ T B STACH/AU
E8             9      PEREZ T C/AU
E9            15      PEREZ T D/AU
E10           32      PEREZ T E/AU
E11            1      PEREZ T FERNANDEZ/AU
E12           28      PEREZ T H/AU

=> s e2-e3
L5           629 ("PEREZ T"/AU OR "PEREZ T A"/AU)

=> e iglesias a v/au
E1            12      IGLESIAS A R/AU
E2             2      IGLESIAS A S/AU
E3             1 --> IGLESIAS A V/AU
E4             1      IGLESIAS AA/AU
E5             2      IGLESIAS ADAM/AU
E6             3      IGLESIAS ADRIANA/AU
E7             1      IGLESIAS AGUSTIN/AU
E8             7      IGLESIAS AINHOA/AU
E9             1      IGLESIAS ALAN/AU
E10           22      IGLESIAS ALBERTO/AU
E11          123      IGLESIAS ALBERTO A/AU
E12            4      IGLESIAS ALBERTO ALVARO/AU

=> e iglesias anna/au
```

```
E1            1      IGLESIAS ANGLES JOSE/AU
E2            2      IGLESIAS ANGLES JOSE M/AU
E3            2 --> IGLESIAS ANNA/AU
E4           89      IGLESIAS ANTONIO/AU
E5            3      IGLESIAS ANTONIO C/AU
E6            7      IGLESIAS ANTONIO CARLOS/AU
E7            1      IGLESIAS ANTONIO CARLOS G/AU
E8            1      IGLESIAS ANTONIO CARLOS GARRIDO/AU
E9            3      IGLESIAS ANTONIO CARLOS R/AU
E10           2      IGLESIAS ANTONIO CARLOS R G/AU
E11          19      IGLESIAS ANTONIO H/AU
E12           1      IGLESIAS ANTONIO J/AU

=> s e3
L6            2 "IGLESIAS ANNA"/AU

=> e moreno r m/au
E1            1      MORENO R JUAN JOSE/AU
E2           27      MORENO R L/AU
E3           49 --> MORENO R M/AU
E4           15      MORENO R M B/AU
E5            2      MORENO R M G/AU
E6            1      MORENO R MA/AU
E7            1      MORENO R NORALBA/AU
E8           13      MORENO R O/AU
E9           24      MORENO R P/AU
E10           1      MORENO R PARADA/AU
E11           1      MORENO R PENA/AU
E12           4      MORENO R R/AU

=> s e3
L7           49 "MORENO R M"/AU

=> d his

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     FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
     LIFESCI' ENTERED AT 09:15:26 ON 08 AUG 2007
L1           10 S ECTEINASCIDIN (W)COMPOUND?
L2            3 S (BACTER? OR CANDIDA?) AND L1
L3            8 DUP REM L1 (2 DUPLICATES REMOVED)
L4            2 S L3 AND RECOMBINANT
                E ESTEBAN B P/AU
                E PEREZ T A/AU
L5          629 S E2-E3
                E IGLESIAS A V/AU
                E IGLESIAS ANNA/AU
L6            2 S E3
                E MORENO R M/AU
L7           49 S E3

=> s l5 or l6 or l7
L8          680 L5 OR L6 OR L7

=> s l3 and l8
L9            0 L3 AND L8

=> d his

     (FILE 'HOME' ENTERED AT 09:08:03 ON 08 AUG 2007)

     FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
     LIFESCI' ENTERED AT 09:15:26 ON 08 AUG 2007
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L1          10 S ECTEINASCIDIN (W)COMPOUND?
L2           3 S (BACTER? OR CANDIDA?) AND L1
L3           8 DUP REM L1 (2 DUPLICATES REMOVED)
L4           2 S L3 AND RECOMBINANT
               E ESTEBAN B P/AU
               E PEREZ T A/AU
L5         629 S E2-E3
               E IGLESIAS A V/AU
               E IGLESIAS ANNA/AU
L6           2 S E3
               E MORENO R M/AU
L7          49 S E3
L8         680 S L5 OR L6 OR L7
L9           0 S L3 AND L8
```

	Document ID	Kind Codes	Source	Issue Date	Pages	Title
1	US 20070154931 A1		US-PGPUB	20070705	299	Genes associate with progression and response in chronic myeloid leukemia and uses thereof
2	US 20060195269 A1		US-PGPUB	20060831	150	Methods and systems for predicting cancer outcome
3	US 20060167228 A1		US-PGPUB	20060727	22	Sequences from an endosymbiont and their uses
4	US 20050181385 A1		US-PGPUB	20050818	387	Synthetic lethal screen using RNA interference
5	US 20050004018 A1		US-PGPUB	20050106	8	Use of antitumoral compound in cancer therapy
6	US 20020137663 A1		US-PGPUB	20020926	13	The anti-neoplastic agent ET-743 inhibits trans activation by SXR
7	US 7247629 B2		USPAT	20070724	207	Antitumoral analogs of et-743
8	US 7241892 B1		USPAT	20070710	95	Hemisynthetic method and new compounds
9	US 7202361 B2		USPAT	20070410	70	Antitumoral ecteinascidin derivatives
10	US 7115743 B2		USPAT	20061003	32	Metabolites of ecteinascidin 743
11	US 6867334 B2		USPAT	20050315	32	Metabolites of ecteinascidin 743 formed by human cytochrome CYP3A4
12	US 6569859 B1		USPAT	20030527	63	Synthetic analogs of ecteinascidin-743
13	US 6348467 B1		USPAT	20020219	61	Synthetic analogs of ecteinascidin-743
14	US 6124292 A		USPAT	20000926	68	Synthetic analogs of ecteinascidin-743
15	US 5750709 A		USPAT	19980512	24	Method and apparatus for isolating therapeutic compositions from source materials

	Document ID	Kind Codes	Source	Issue Date	Pages	Title
1	US 20060167228 A1		US-PGPUB	20060727	22	Sequences from an endosymbiont and their uses
2	US 20060134764 A1		US-PGPUB	20060622	73	Gene cluster involved in safracin biosynthesis and its uses for genetic engineering
3	US 20060111570 A1		US-PGPUB	20060525	127	Synthetic process for the manufacture of an ecteinaschidin compound
4	US 20060019960 A1		US-PGPUB	20060126	237	Antitumoral analogs of ET-743
5	US 20040019056 A1		US-PGPUB	20040129	187	Anititumoral analogs of et-743
6	US 20040002602 A1		US-PGPUB	20040101	122	Synthetic process for the manufacture of an ecteinaschidin compound
7	US 7247629 B2		USPAT	20070724	207	Antitumoral analogs of et-743
8	US 7241892 B1		USPAT	20070710	95	Hemisynthetic method and new compounds

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	L #	Hits	Search Text
1	L1	50	ecteinascidin adj5 compound$3
2	L2	254205	bacteri$3 or candida
3	L3	15	(recombinant or "DNA") same l1
4	L4	0	l2 same l3
5	L5	17557	ESTEBAN PEREZ IGLESIAS MORENO
6	L6	8	l1 and l5